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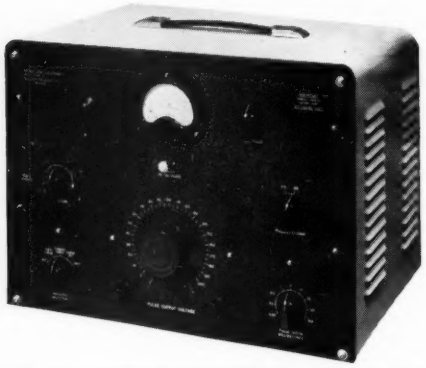

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# ANNALS OF PHYSICAL MEDICINE

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Vol. V November 1959 No. 4

ORIGINAL PAPER

## THE VALUE OF MUCOPROTEIN LEVELS AND OTHER SEROLOGICAL REACTIONS IN RHEUMATOID ARTHRITIS

### A PRELIMINARY REPORT*

BY CHARLOTTE FELDMAN, EVELYN V. HESS, AND R. L. MARKHAM

*From the Department of Physical Medicine and Rheumatology, Royal Free Hospital, London*

THE need for a serological test as a reliable index of activity in rheumatoid disease, and preferably specific for that disease, has become more obvious since the introduction of systemic steroid therapy. Although the erythrocyte sedimentation rate is generally used for this purpose, it is both non-specific and an unreliable measure of disease activity in untreated and treated cases alike (Lawrence, 1953).

In an attempt to find a reliable test two of the so-called "acute-phase reactions"—namely, serum mucoproteins and C-reactive protein—were investigated. The serum mucoproteins are defined by their solubility in acid protein precipitants, a high proportion of bound carbohydrate, and low isoelectric points. C-reactive protein, which is not found in the serum of normal persons, is defined by its specific reaction with the polysaccharide of C-pneumococcus. Both substances show raised levels in the serum of patients with necrotic or inflammatory processes.

The technique for the estimation of mucoproteins used in this investigation (see below) enables separate determinations to be made of two fractions which

* Paper read at the Annual Meeting of the British Association of Physical Medicine, April 26, 1958.

together account for almost all mucoprotein present in the serum. An earlier survey based on single estimations (Jacobs and Markham, 1957) made it clear that a more profitable approach to the study of the relationships between the levels of these substances and the disease process would be by serial investigations over a prolonged period on a number of carefully classified patients. Thus these serological tests have been carried out and correlated with the erythrocyte sedimentation rate and serial clinical assessments.

In view of the long-term follow-up embarked upon, the Rose–Waaler sheep-cell agglutination test was included in the serial evaluations so as to investigate its possible value in prognosis (Duthie *et al.*, 1957). However, since no trends are apparent at this early stage, our observations will be recorded in a later report.

## METHOD

Only patients under 65 years of age with uncomplicated rheumatoid arthritis, who had not received phenylbutazone, gold salts, or systemic adrenocorticosteroids in the preceding six months, were included. Clinical classification of the rheumatoid state into one of four stages was made according to the American Rheumatism Association's criteria (Steinbrocker, Traeger, and Batterman, 1949), with subdivision into four groups of disease activity based on the number of active joints. Monthly clinical assessments were carried out along the lines laid down by the Empire Rheumatism Council (1955), blood being collected on each occasion for the required serological tests.

The two mucoprotein fractions, so-called M.1 and M.2, were estimated by a modification of the zone electrophoretic technique described by Markham, Jacobs, and Fletcher (1956), and their levels were recorded in arbitrary units. C-reactive protein was measured by the precipitin method of Anderson and McCarty (1950), and erythrocyte sedimentation rates in the first hour by the method of Westergren.

## RESULTS

Eight months after starting this study sufficient monthly observations to warrant inclusion in a preliminary report have been made on 23 patients, of whom 12 were female and 11 male.

### Erythrocyte Sedimentation Rate

As expected, the distribution of E.S.R. values was essentially similar in the different stages of the disease, while grouping according to degree of activity (Fig. 1) revealed a definite upward trend with increasing activity. However, the

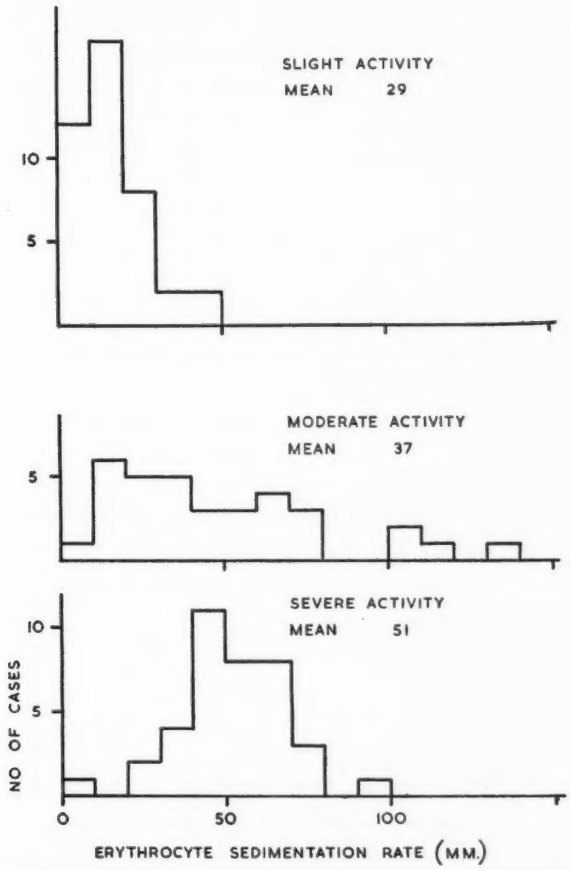


FIG. 1.—Distribution of E.S.R. values among patients grouped according to degree of rheumatoid activity.

very wide range of values noted, particularly in the moderately active group, confirmed the unreliability of the E.S.R. as an index of activity.

## C-REACTIVE PROTEIN

The range of values was 0-12 units and their distribution was found to be similar in the different disease stages. The histograms (Fig. 2) of C-reactive protein levels in patients grouped according to the degree of rheumatoid activity show lower mean values in less active disease, but over half the indi-

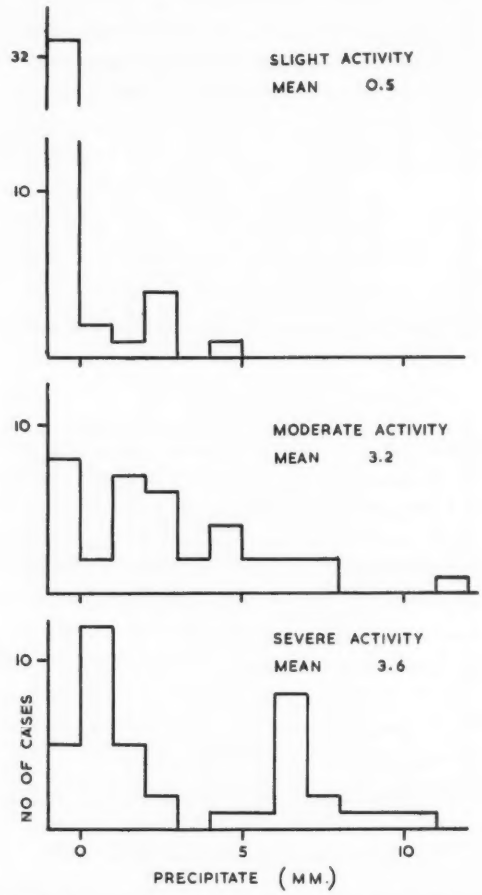


FIG. 2.—Distribution of C-reactive protein levels among patients grouped according to degree of rheumatoid activity.

vidual readings in the more active group fall within the range covered by the majority of values found in patients with slighter disease activity.

## MUCOPROTEINS

Initially mucoprotein levels were estimated in 10 healthy adults selected for similarity in age (30-65 years) to the rheumatoid group. In health the range of M.1 was 5-22 with a mean of 15 units; and for M.2, 10-26 with a mean of 20 units. In the rheumatoid series M.1 ranged up to 90 and M.2 to 250 units.

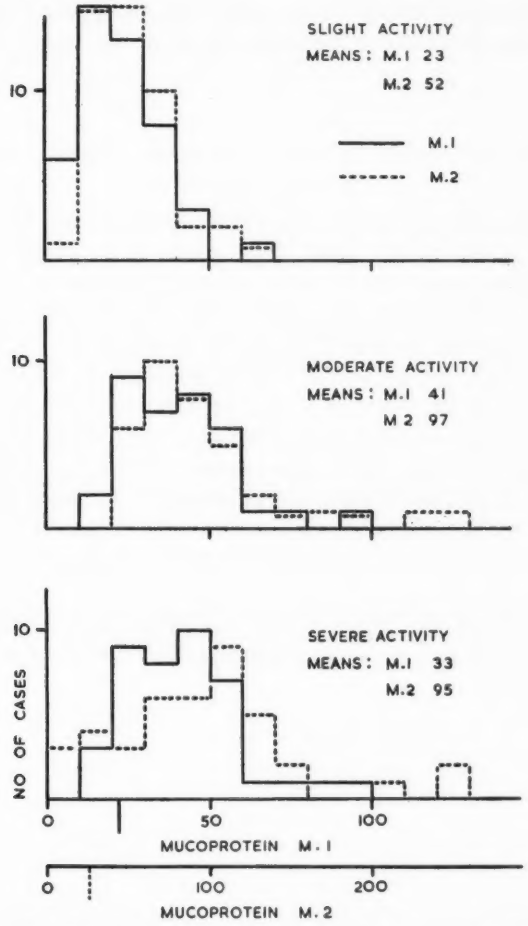


FIG. 3.—Distribution of mucoprotein levels among patients grouped according to degree of rheumatoid activity. The lines on the mucoprotein scales indicate the upper limits of normal values.

In the different stages of the disease a similar distribution of mucoprotein values was found, except that the highest levels were associated with more advanced disease.

When mucoprotein levels were plotted for similar degrees of activity regardless of disease stage, an extension of range was found in the moderately and severely active groups, the mean value showing considerable increase in

the former without further rise in the latter. The histograms (Fig. 3) illustrate this and also show similarity in the behaviour of the two mucoprotein fractions M.1 and M.2.

## Correlation of Serological Changes with Variations in Clinical Activity

Five patients with inactive or only slightly active disease had no C-reactive protein in the serum at any time. However, in many of the other patients C-reactive protein values showed wide variations apparently unrelated to the degree of joint activity. Thus, in a patient with long-standing Stage III disease (Fig. 4) the C-reactive protein level fluctuated between zero and one unit, although clinically severe joint activity, associated with an E.S.R. of 40-60 mm. and moderately high mucoprotein levels, was observed throughout. In another patient with less long-standing Stage III disease (Fig. 5) very wide variations of the C-reactive protein level accompanied severe but unchanging joint activity, an E.S.R. of 100-140 mm., and persistently high values for the M.1 and M.2 fractions. An example of clinically "burnt-out" Stage III disease is shown in Fig. 6; here M.1 is within normal limits, while M.2 is persistently though only slightly raised.

Altogether six of our patients—four with slight disease activity and two with inactive disease—showed normal values of M.1 sustained over a period of

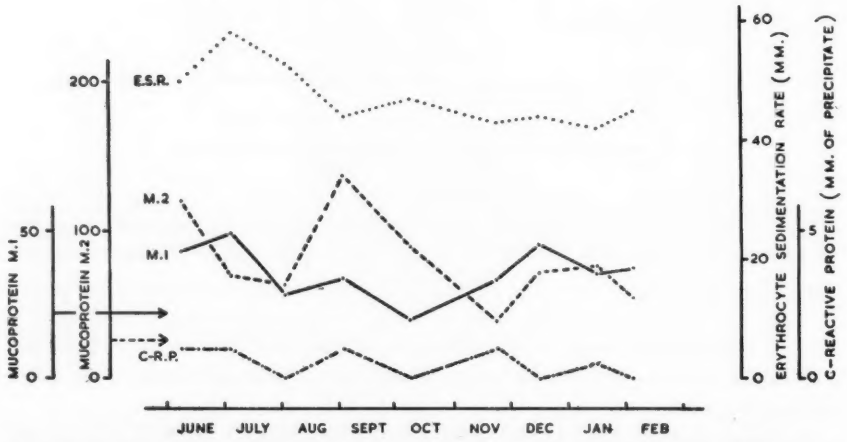


FIG. 4.—Serial readings of acute-phase reactants in a case of chronic Stage III disease with maintained severe joint activity. The arrows on the mucoprotein scales indicate the upper limits of normal values.

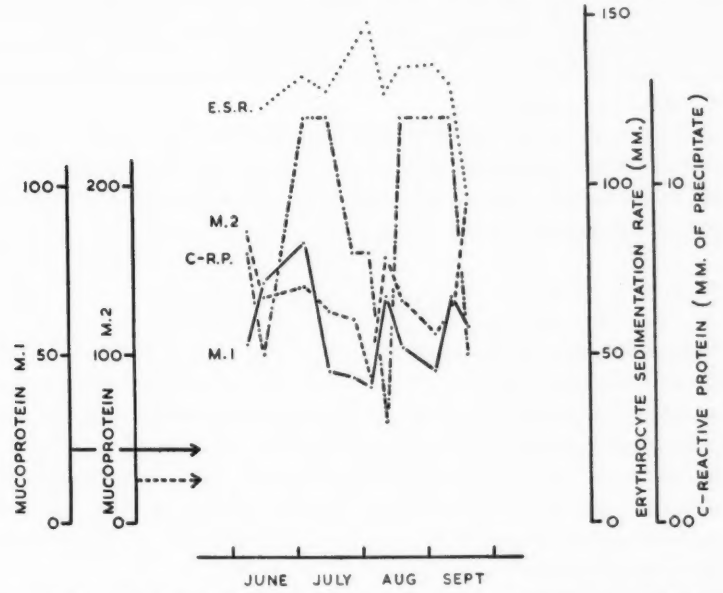


FIG. 5.—Serial readings of acute-phase reactants in a case of acute Stage III disease with maintained severe joint activity. The arrows on the mucoprotein scales indicate the upper limits of normal values.

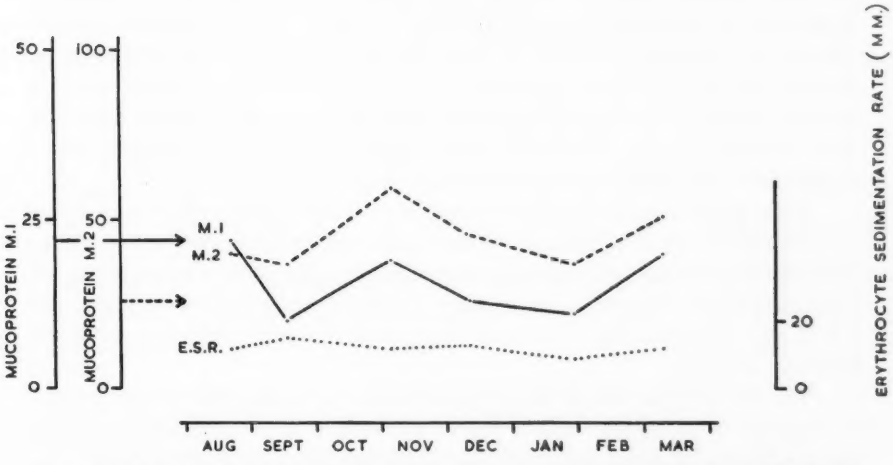


FIG. 6.—Serial readings of acute-phase reactants in a case of inactive Stage III disease. C-reactive protein was absent on all occasions. The arrows on the mucoprotein scales indicate the upper limits of normal values.

at least two months, while the level of fraction M.2 remained elevated. In a further seven patients showing moderate or severe activity, M.1 values returned to within normal limits on single occasions without a corresponding return of the M.2 level to normal.

In the two cases with active disease illustrated in Figs. 4 and 5 wide variations of the raised mucoprotein levels are seen in the absence of noteworthy changes in the clinical picture, the latter being reflected more accurately by the relatively stable E.S.R.

## DISCUSSION

It must be pointed out that neither of the two mucoprotein fractions estimated in this investigation corresponds to the seromucoid fraction isolated by Winzler's (1955) technique, or variations of it. Investigations (to be published) have shown that the seromucoid fraction consists of an almost completely recovered fraction M.1 (which is identical with the carbohydrate-rich orosomucoid) and a portion only of fraction M.2. Therefore an accurate comparison cannot be made between the mucoprotein levels obtained by Winzler's technique and those reported in this paper.

The absence of any close correlation between clinical activity and the levels of the three acute-phase reactants can be analysed into: (1) unaccountable variations in levels shown in individual patients (frequently by C-reactive protein, less so by mucoproteins, and only rarely by the E.S.R.); and (2) the persistent differences in the levels of these substances found in patients grouped together because of apparent similarity in both disease stage and activity. The latter finding has tempted us to speculate on possible differences in the underlying disease process, and it is hoped that the final analysis, taking into account the type of joints affected, systemic features, radiological findings, and the Rose–Waaler test, will yield more information on this point.

During the comparatively short period covered by this preliminary report no spontaneous or drug-induced remissions have been observed. It has, therefore, not been possible to compare the value of these indices in reflecting or predicting major changes in the clinical picture, while in minor variations the E.S.R. and mucoproteins have been found to be of apparently equal though limited usefulness.

The levels of the two mucoprotein fractions show parallel changes except for a tendency of fraction M.2 to remain elevated in some cases with clinically inactive disease; it is not possible as yet to discern any significance in this.

During this initial period it has been one of the objects of our investigation to obtain a base line with which to compare the pattern of the levels obtained

with various forms of therapy. Aspirin has been the only drug administered during this time, and in the dosages normally used in rheumatoid arthritis no appreciable effect on the serological tests under investigation was noted.

## SUMMARY

A preliminary report dealing with an evaluation of some "acute-phase reactions" in rheumatoid disease is presented. In view of the shortness of the investigation to date, observations in major clinical changes, both spontaneous and drug-induced, are not included.

In assessing rheumatoid activity, isolated estimations of these indices were found to be disappointing. Serial readings of mucoproteins and erythrocyte sedimentation rate levels were more satisfactory than C-reactive protein, but also of limited value.

It will be of interest to study these serological reactions in spontaneous and drug-induced remissions, and to investigate the significance of persistently raised M.2 mucoprotein levels in "burnt-out" disease.

Maintained differences in these indices in patients with clinically similar disease suggest the possibility of different underlying disease processes.

### ACKNOWLEDGMENT

We are grateful to Dr. A. T. Richardson for his encouragement and advice throughout this investigation.

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ORIGINAL PAPER

# 6-α-METHYL PREDNISOLONE IN THE TREATMENT OF RHEUMATOID ARTHRITIS

By MALCOLM THOMPSON

*From the Department of Physical Medicine, Royal Victoria Infirmary, Newcastle upon Tyne*

THE introduction of prednisone and prednisolone in 1955 (Bunim *et al.*) represented a major advance in the search for potent anti-inflammatory steroids free from undesirable side-effects, and these predni-steroids became established as the agents of choice when systemic steroid therapy was indicated in the treatment of rheumatoid arthritis. In 1956 two further synthetic steroids were prepared—9-α-fluoro-16-hydroxy-prednisolone, known as triamcinolone (Bernstein *et al.*, 1956) and 6-α-methyl prednisolone (Lyster *et al.*, 1957). The latter compound, which differs from prednisolone only in the substitution of a methyl group for a hydrogen atom at the 6-α position, is the subject of this report.

Although assays on animals indicated that 6-α-methyl prednisolone was twice as potent as prednisolone in respect of anti-inflammatory activity (Lyster *et al.*, 1957), clinical trials conducted by Boland and Liddle (1957) did not show any advantage over prednisolone either in potency or in pattern of side-effects. However, Bilka and Melby (1958) and Montgomery (1958) found 6-α-methyl prednisolone to be 25% more potent, milligramme for milligramme, than prednisolone, and Grater (1958) considered it to be one and a half times more effective in the treatment of allergic disorders.

Triamcinolone has received more attention and has been available in the United Kingdom for a longer period than 6-α-methyl prednisolone. Recent reports have emphasized several undesirable side-effects of triamcinolone (Kendall and Hart, 1959; Robinson and Robinson, 1959; Thompson, 1959; and Williams, 1959). As it is useful to have alternative effective steroid preparations, the clinical properties of 6-α-methyl prednisolone have been studied in a trial devised to compare its potency with that of prednisolone and of triamcinolone, and to determine whether its initial side-effects were qualitatively or quantitatively different, in the treatment of rheumatoid arthritis.

## METHOD OF TRIAL

Fourteen patients (10 women and 4 men) suffering from rheumatoid arthritis and "stabilized" on prednisolone therapy were transferred to triamcinolone, and subsequently to 6-α-methyl prednisolone. In some instances there

was an interim period of further prednisolone therapy between treatment with triamcinolone and with 6-α-methyl prednisolone. The dosage ratios maintained were those of 5 : 4 in milligrammes between prednisolone and triamcinolone and between prednisolone and 6-α-methyl prednisolone. Dosage ranged from 5 to 20 mg. daily expressed as prednisolone, the average being 11 mg. Serial measurements were taken of hand grip, blood-pressure, weight, and erythrocyte sedimentation rate (Westergren), in addition to listing of the joints involved, assessments of disease activity and functional capacity, and the patient's own impression of improvement. The methods and criteria of improvement have been described elsewhere (Thompson, 1959). In all patients the minimum period of treatment with each steroid was two weeks, and in the majority it considerably exceeded this period. As the available preparation of 6-α-methyl prednisolone consisted of tablets of a distinctive shape (Medrone, Upjohn) the patients were informed that they were receiving a new preparation of prednisolone, but no suggestion was made that this preparation differed in any other way from that drug.

## RESULTS

These are summarized in the Table, and do not show any pronounced difference between the three steroids. In terms of relief of pain and stiffness, triamcinolone was the most useful agent in 4 out of 14 cases, Medrone in 3 out of 14, and prednisolone in 2 out of 14, with 5 patients finding no appreciable difference between the three drugs. None of the patients showed any significant improvement in functional capacity, and disease activity diminished in only two cases—one during prednisolone and the other during Medrone therapy. No great difference was seen in respect of the power of grip or of the E.S.R. during treatment with the three steroids. The patients' own preferences were weighted slightly in favour of triamcinolone, four patients having an exclusive preference for this compound, and a fifth patient considered it to be of equal merit with Medrone and superior to prednisolone; three patients had an exclusive preference for prednisolone, and two for Medrone.

The side-effects listed in the Table are those caused predominantly or exclusively by Medrone in comparison with the other two steroids. The two most prominent side-effects during Medrone therapy were digestive disorders and ecchymoses, but no serious side-effects were observed, and of three patients suffering from dyspepsia there was only one patient with severe dyspepsia and vomiting, and there was no radiological evidence of peptic ulceration in this case. Subcutaneous ecchymoses were seen in two patients, as described by Nashelsky and Smyth (1958), but were not serious and were not associated with

any abnormal haematological findings. Although severe "moon-face" with flushing developed in one patient during Medrone therapy and persisted with subsequent triamcinolone and prednisolone treatment, there were two instances in which these signs, provoked by triamcinolone, were ameliorated by Medrone.

TABLE SUMMARIZING RESULTS

| Patient's No. and Sex | Duration of Treatment in Weeks | Joint Pains | Stiffness | Functional Capacity | Disease Activity | Grip | E.S.R. | Adverse Side-effects | Beneficial Effects | Patient's Preference |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 F | 3 | Tri. | Tri. | 0 | 0 | Tri./Pred. | 0 | Nil | Less moon-face, perspiration, and flushing than with Tri. | Tri. |
| 2 M | 3 | Tri. | Tri. | 0 | 0 | Tri. | Med./Tri. | Nil | Nil | Tri. |
| 3 F | 2 | Tri. | Tri. | 0 | 0 | Tri. | 0 | Dyspepsia and vomiting | Less moon-face, perspiration, and flushing than with Tri. | Tri. |
| 4 F | 3 | Pred. | Pred. | 0 | 0 | Tri./Pred. | 0 | Nil | Nil | Pred. |
| 5 F | 12 | 0 | 0 | 0 | 0 | 0 | Tri. | Nil | Nil | 0 |
| 6 F | 6 | 0 | 0 | 0 | 0 | 0 | 0 | Ecchymosis | Nil | 0 |
| 7 M | 5 | Med. | Med. | 0 | 0 | 0 | Pred./Med. | Nil | Nil | Med. |
| 8 F | 2 | Tri. | Tri. | 0 | 0 | 0 | 0 | Nil | Nil | Tri. |
| 9 F | 4 | 0 | 0 | 0 | 0 | 0 | 0 | Nil | Nil | 0 |
| 10 F | 4 | Med. | Med. | 0 | 0 | Med. | Tri. | Dyspepsia | Nil | Med./Tri. |
| 11 F | 3 | Pred. | Pred. | 0 | Pred. | Pred./Med. | Pred. | Ecchymosis | Nil | Pred. |
| 12 M | 2 | 0 | 0 | 0 | 0 | 0 | Med./Tri. | Dyspepsia and vomiting | Nil | Pred. |
| 13 M | 32 | Med. | Med. | 0 | Med. | 0 | Med. | Nil | Nil | Med. |
| 14 F | 6 | 0 | 0 | 0 | 0 | Med. | 0 | Moon-face | Nil | 0 |

Tri. = triamcinolone.
Pred. = prednisolone.
Med. = 6-α-methyl prednisolone (Medrone).
0 = no striking difference.

In respect of effect upon blood pressure, there was no evidence that Medrone causes a fall in blood pressure or that its effect was any different from that of prednisolone, whereas in three patients with hypertension there appeared to be a significant fall in blood pressure during triamcinolone therapy, and in a further four patients lowest blood-pressure readings were recorded during triamcinolone therapy. The remaining seven patients had approximately equal blood-pressure readings during treatment with all three steroids.

With regard to loss of weight, only variations of 2 lb. or over were considered significant, and the greatest losses were seen with triamcinolone therapy. In seven patients there was significant weight loss exclusively with triamcinolone. One patient lost 2 lb. in weight during prednisolone therapy, and six patients showed no striking differences.

## DISCUSSION

After a decade of steroid therapy the place and value of these compounds in the management of rheumatoid arthritis are still not precisely defined. While long-term trials of cortisone and prednisolone should provide answers to some of the problems, the position has become recently complicated by the introduction of three further anti-inflammatory steroids. Two of these, triamcinolone and Medrone, have been stated to be clinically 25% more potent, weight for weight, than prednisolone, and the present trial lent some confirmation to this view, although it was clear that the ratio varied, and in some patients identical dosage in milligrammes was required to give comparable relief with Medrone and prednisolone. The third and most recent steroid is also a predni-steroid, being 9-α-fluoro-16-α-methyl prednisolone, known as dexamethasone (Boland, 1958), and is reputed to be between seven and ten times more potent than prednisolone (Bunim *et al.*, 1958). However, anti-inflammatory potency alone is not an adequate test of a new steroid, the incidence and severity of adverse side-effects being the most important factors.

Several recent reports have stressed the frequency of side-effects, especially muscle wasting and myopathy, with triamcinolone, and MacLean and Schurr (1959) described muscular paralysis similar to triamcinolone myopathy in a patient who had received treatment with fluorocortisone, which, like triamcinolone, contains a fluorine atom in the 9-α position. Should the incorporation of this fluorine atom prove to be the factor responsible for the myopathy, then dexamethasone may, in turn, be capable of producing this side-effect. Medrone, although not so potent as dexamethasone, deserves some attention, as it does not contain the 9-α-fluoro configuration and is composed exclusively of carbon, hydrogen, and oxygen.

Although it is now possible to predict the biological activity of a synthetic steroid on the basis of its chemical structure, quantitative assessments of the potency and properties of these new compounds, based on experiments with laboratory animals, have not been substantiated in clinical practice. Thus, the work of Lyster *et al.* (1957) suggesting that Medrone was twice as potent as prednisolone in respect of anti-inflammatory activity has not been borne out in this or any other clinical trial. Similarly, with regard to side-effects, these

may to a certain extent be predicted on the basis of special molecular constructions in the steroid formula, but earlier hopes that, in particular, the gastro-intestinal, diabetic, and osteoporotic side-effects had been dissociated from the anti-inflammatory effect have not been realized. The predni-steroids, with a double bond in the 1 : 2 position, represented a major advance in therapy by giving an enhanced anti-inflammatory effect with less severe mineralocorticoid effects. Prednisone and prednisolone became, as a result, the steroids of choice when steroid therapy was indicated in rheumatoid arthritis. There is no evidence from this trial to indicate that Medrone differs greatly from prednisolone, and it cannot be considered to supersede prednisolone as the steroid agent of choice. Triamcinolone, despite the disadvantages already enumerated, has been shown to be useful for patients with hypertension and oedema, especially when these symptoms have been aggravated by previous prednisolone treatment. The place of dexamethasone has still to be established, but early reports of severe gastro-intestinal side-effects (Fearnley, 1959) and ecchymoses (Bunim *et al.*, 1958) suggest that dexamethasone is similar to other predni-steroids in the pattern of side-effects. Fortunately these side-effects are not reproduced exactly between one steroid and another, so that these extra compounds are sometimes useful when complications arise during steroid therapy, and may be helpful in allowing the dosage to be gradually reduced when this is required.

The indications for steroid therapy in the management of rheumatoid arthritis have not been altered by the introduction of these new steroids. Short-term trials, of the type described in this paper, can be helpful in quickly assessing the place of a new steroid compound in relation to prednisolone, which may be taken as a standard, but these short-term trials do not in any way supersede or replace the long-term studies presently being conducted into the effects and value of prednisolone.

## SUMMARY

Fourteen patients suffering from rheumatoid arthritis and receiving treatment with prednisolone were subsequently treated with 6-α-methyl prednisolone (Medrone) and with triamcinolone. The duration of treatment with Medrone varied from 2 to 32 weeks, and the dosages ranged from 4 to 16 mg. daily.

No striking difference was observed between prednisolone and Medrone, and although Medrone was generally as effective as prednisolone in a dosage ratio of 4 : 5, in several patients equal dosage was required to produce an equivalent therapeutic effect. Mild dyspeptic symptoms developed during Medrone therapy in three patients who had tolerated prednisolone without dyspepsia. A fall in blood pressure and weight loss, noted in 50% of the

patients during triamcinolone therapy, did not occur during treatment with Medrone.

It is considered that Medrone is not superior to prednisolone in the management of rheumatoid arthritis, but that it may be useful as an alternative steroid preparation in the event of side-effects developing during prednisolone therapy.

ACKNOWLEDGMENT

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ORIGINAL PAPER

# REHABILITATION OF MALLEOLAR FRACTURES OF THE TIBIA AND FIBULA

BY P. J. R. NICHOLS and J. G. PARISH*

*From the Royal Air Force Medical Rehabilitation Units, Chessington and Collaton Cross*

THE results of rehabilitation of patients with fractures of the shafts of the tibia and fibula at Royal Air Force Rehabilitation Centres have been analysed in a previous paper (Nichols and Parish, 1959). It was found that the value of early transfer to rehabilitation centres appeared to be in the prevention and correction of faulty walking patterns in plaster, and in having patients available for intensive treatment during the immediate post-plaster phase. Patients arriving later than the third post-plaster week required considerably longer periods of treatment than the remainder. This difference appeared to be due to the increased incidence and delay in dispersion of oedema. The purpose of the present paper is to present the results of a similar rehabilitation programme in patients with malleolar fractures of the tibia and fibula.

## CLASSIFICATION OF FRACTURES

The classification of ankle fractures according to the mechanism of production (Bonnin, 1950; Lauge-Hansen, 1950) proved to be impracticable, as the patients were referred to us some time after injury, and essential information for detailed classification could not always be obtained from a patient's notes or radiographs. Similarly, the partly anatomical and partly mechanistic classification introduced by Watson-Jones (1955) did not prove suitable for this survey. We have therefore adopted a classification based on the anatomical site of the fracture.

Fractures of the fibula have been divided into three groups on the lines of an anatomico-pathological classification suggested by Ashhurst and Bromer (1922), according to whether the site is above, between, or below the inferior tibio-fibular ligaments. The anterior and posterior inferior tibio-fibular ligaments are attached to corresponding tubercles of the tibia and fibula. Hence the terms supratubercular, intertubercular, and infratubercular or basal fractures of the fibula have been introduced to describe the three groups (Parish, 1957). Fractures of the tibia involving the ankle-joint have been divided into fractures of the medial malleolus, of the anterior margin, and of

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the posterior malleolus. The terms bimalleolar and trimalleolar fractures have been used to describe the combination of two or three malleolar fractures, after the practice of Speed (1914), MacKinnon (1928), Ollerenshaw (1929), and Henderson (1932).

The complete classification of ankle fractures (see below) also includes sprain or avulsion fractures in which a small bone flake is avulsed from one or more malleoli; epiphysial separation fractures occurring in adolescents before the epiphyses are united; and compression fractures of the shaft of the tibia involving the ankle-joint.

### Classification of Ankle Fractures

I. Sprain Fractures

Avulsion of the tip of lateral or medial malleolus or both; flake fracture of the anterior margin of the fibula; fractures of the anterior tubercles of tibia or fibula; posterior marginal flakes.

II. Isolated Fractures (Unimalleolar)

1. Medial malleolus
2. Lateral malleolus
   - Basal
   - Intertubercular
   - Supratubercular
3. Posterior margin (or malleolus)
4. Anterior margin

III. Bimalleolar Fractures

1. Medial and lateral malleoli
2. Posterior and lateral malleoli
3. Posterior and medial malleoli

IV. Trimalleolar Fractures

V. Compression Fractures of Lower Third of Tibia

T- and Y-shaped and spiral fractures into the ankle-joint, and comminuted fractures of the articular surface of the tibia.

VI. Epiphysial Separation Fractures

## METHOD OF TREATMENT

The method of treatment of ankle fractures at the R.A.F. Rehabilitation Centres is similar to that of shaft fractures of the tibia and fibula described in a previous paper (Nichols and Parish, 1959). Patients with both types of fracture are treated together according to a programme based on class exercises and remedial games lasting six hours per day. The patients are divided into

three groups depending on the grade of activity permitted. In the early group attention is paid to walking correctly either in plaster or in the immediate post-plaster stage. In the intermediate and advanced groups calf-muscle power and spring are developed until the patient is able to run and jump without difficulty.

## THE SERIES

The results and opinions expressed in this paper are based on a study of the medical records of 191 patients: (*a*) those treated at R.A.F. Medical Rehabilitation Unit, Chessington, between October, 1946, and December, 1953=109 cases; and (*b*) those treated at R.A.F. Medical Rehabilitation Unit, Collaton Cross, between January, 1953, and December, 1956=82 cases.

TABLE I

DETAILS OF THE SERIES

| | Percentage |
|---|---|
| Age Range: | |
| Under 20 years | 40 |
| 20–30 years | 50 |
| Over 30 years | 10 |
| Causes of Accident: | |
| Motor-cycle accidents | 20 |
| Other road accidents | 4 |
| Football | 18 |
| Rugby football | 8 |
| Gymnastics | 5 |
| Assault and battle training | 8 |
| Parachute jumping | 3 |
| Other causes | 34 |
| Disposal: | |
| Full duty | 84 |
| Modified duty | 14 |
| Invalided | 2 |

The fractures studied are shown in Table II.

TABLE II

FRACTURES STUDIED

| | No. of Cases |
|---|---|
| Unimalleolar: | |
| Lateral malleolus only | 87 |
| Medial malleolus only | 34 |
| Bimalleolar: | |
| Lateral and posterior | 20 |
| Lateral and medial | 26 |
| Trimalleolar | 24 |
| Total | 191 |

### Fractures Excluded

Fractures of the ankle excluded from this study because of their infrequency or relative insignificance were: avulsion ("sprain") fractures; isolated fractures of the anterior margin or posterior malleolus; bimalleolar fracture of medial and posterior malleoli; compression fractures; ankle fractures complicated by other fractures of the lower limbs; and epiphysial separation fractures.

#### AVULSION FRACTURES

Avulsion or "sprain" fractures required about three weeks in plaster followed by a further three weeks' mobilization at the rehabilitation centre. Permanent disability has not occurred in any of our patients. We have found that these fractures often do better than simple sprains, probably because they are treated more seriously. Collateral ligament injuries treated in the same way give similar results.

In this series the presence of an avulsion fracture or a ligamentous injury in addition to a malleolar fracture did not increase the time in plaster or the mobilization period. The results of treatment are therefore presented according to the type of malleolar fracture alone.

## RESULTS

The time of application of a walking plaster and the time of removal of plaster were both very variable, depending on the views of the medical officer supervising treatment at the time. The diagnosis of clinical union depends mainly on the absence of pain on local pressure and attempted compression of the malleoli.

Table III shows the tendency for open reduction in bimalleolar and trimalleolar fractures to be associated with some delay in clinical union. This is presumably because the severer fractures are more likely to be subjected to operation. Isolated fractures of the lateral malleolus united quickly, although those fractures of the fibula above the inferior tibio-fibular ligaments (supratubercular fractures) took an average of nine weeks to unite, compared with an average of six weeks for intertubercular fractures.

### Mobilization Time

The term "mobilization time" describes the time from the removal of plaster until the patient is fit for discharge. In this series the time was very variable, as some medical officers tended to mobilize ankle fractures much earlier than did others. Thus the total time of disability is probably a more accurate parameter to study than the mobilization time. This is in contrast to

TABLE III

ANALYSIS OF TIME FOR CLINICAL UNION IN PATIENTS WITH ANKLE FRACTURES ACCORDING TO TYPE OF FRACTURE AND TYPE OF REDUCTION

| Type of Fracture | No. of Patients | Time for Clinical Union in Weeks | | | | Total |
|---|---|---|---|---|---|---|
| | | 4–7 | 8–11 | 12–15 | 16–20 | |
| | | % | % | % | % | % |
| Unimalleolar: | | | | | | |
| Lateral malleolus (closed) .. | 87 | 63 | 35 | 2 | — | 100 |
| Medial malleolus: | | | | | | |
| Closed reduction .. .. | 22 | 45 | 50 | 5 | — | 100 |
| Open reduction .. .. | 12 | 42 | 50 | 8 | — | 100 |
| Bimalleolar: | | | | | | |
| Lateral and posterior (closed) .. | 20 | 10 | 90 | — | — | 100 |
| Lateral and medial: | | | | | | |
| Closed reduction .. .. | 17 | 41 | 29 | 24 | 6 | 100 |
| Open reduction .. .. | 7 | — | 33 | 67 | — | 100 |
| Trimalleolar: | | | | | | |
| Closed reduction .. .. | 17 | 29 | 53 | 18 | — | 100 |
| Open reduction .. .. | 6 | — | 57 | 14 | 29 | 100 |
| All cases .. .. .. .. | 188 | 44 | 46 | 8 | 2 | 100 |

TABLE IV

ANALYSIS OF AVERAGE TIME FOR CLINICAL UNION AND MOBILIZATION

| Type of Fracture | No. of Cases | Average Time for Clinical Union in Weeks | Average Mobilization Time in Weeks | Average Total Disability Time in Weeks |
|---|---|---|---|---|
| Unimalleolar: | | | | |
| Lateral malleolus (closed reduction only) .. | 87 | 6 | 6 | 12 |
| Medial malleolus: | | | | |
| Closed reduction .. .. | 22 | 6 | 6 | 12 |
| Open reduction .. .. | 12 | 8 | 7 | 15 |
| Bimalleolar: | | | | |
| Lateral and posterior (closed reduction only) .. | 20 | 7 | 10 | 17 |
| Lateral and medial: | | | | |
| Closed reduction .. .. | 17 | 11 | 8 | 19 |
| Open reduction .. .. | 7 | 12 | 13 | 25 |
| Trimalleolar: | | | | |
| Closed reduction .. .. | 17 | 9 | 11 | 20 |
| Open reduction .. .. .. | 6 | 14 | 12 | 26 |

the findings in our previous survey of fractures of the shafts of the tibia and fibula.

Table IV reflects a tendency to retain plaster splintage longer after open reduction; whether this is in deference to orthopaedic opinion or lack of confidence in the powers of surgery, or because surgery was undertaken only in the more severe cases, is not clear.

## Total Disability Time

Table V illustrates the manner in which the total disability time increases with further bone damage. Bimalleolar fractures involving the medial malleolus show an increased disability time compared with those involving the lateral and posterior malleoli, and fare no better than trimalleolar fractures. The development of post-plaster oedema extends the disability period by some four weeks.

TABLE V

Summary of Factors Affecting the Total Disability Time after Ankle Fractures

| | Average Total Disability Time in Weeks |
|---|---|
| 1. Type of fracture: | |
| Lateral malleolus only | 12 |
| Medial malleolus only | 13 |
| Lateral and posterior malleoli | 17 |
| Lateral and medial malleoli | 21 |
| Trimalleolar fractures | 21 |
| 2. Type of reduction: | |
| Closed reduction | 14 |
| Open reduction | 16 |
| 3. Post-plaster oedema: | |
| Without oedema | 12 |
| With oedema | 16 |

## Type of Reduction

Open reduction was associated with some slight increase in the disability time in fractures of the medial malleolus and bimalleolar fractures, but open reduction was probably carried out in the more severe fractures.

## Time of Transfer to Rehabilitation Unit

A full analysis of the records of the total disability period was made according to the type of fracture, the time of transfer to the rehabilitation unit

TABLE VI

TOTAL DISABILITY TIME AFTER ANKLE FRACTURES ACCORDING TO TYPE OF REDUCTION AND TYPE OF FRACTURE

| Type of Fracture | Total Disability Time in Weeks | |
|---|---|---|
| | Closed Reduction | Open Reduction |
| Lateral malleolus only .. .. .. | 12 | — |
| Medial malleolus only .. .. .. | 12 | 15 |
| Lateral and posterior malleoli .. .. | 17 | — |
| Lateral and medial malleoli .. .. .. | 19 | 25 |
| Trimalleolar fractures .. .. .. | 20 | 26 |

in relation to clinical union, and the type of reduction. The average total disability time for unimalleolar fractures was 12 weeks and for trimalleolar fractures 21 weeks, whether the patient was transferred before or after clinical union. For bimalleolar fractures the average total disability time for cases transferred early was 15 weeks, and for those transferred after clinical union it was 18 weeks. Thus treatment in plaster resulted in slightly more rapid recovery in the bimalleolar fracture group, but not in the remaining groups.

In a detailed analysis of 132 ankle fractures (Parish, 1957) delay in starting full-time rehabilitation was associated with a more prolonged disability period. The patients were divided into four groups according to whether they had been treated in plaster for (*a*) over 28 days or (*b*) less than 28 days, or whether they arrived for rehabilitation (*c*) within 14 days of removal of the plaster or (*d*) later than this period. The most important period for rehabilitation seems to be the first two or three weeks of mobilization, since the patients who arrived later than 14 days after the removal of the plaster were, on an average, a month longer under treatment than all other groups in which the treatment time was similar. In patients in whom clinical union was delayed the effect of delay in instituting in-patient rehabilitation was more marked.

## POST-PLASTER OEDEMA

The over-all incidence of post-plaster oedema in our series of 555 cases of fractures of the shafts of the tibia and fibula was 23%; in this series of fractures of the ankle the over-all incidence was 33%. However, there was not the same association of osteoporosis and persistent oedema, for only two cases of severe osteodystrophy were recorded in the present series. As with shaft fractures, open reduction was accompanied by a marked increase in the incidence of oedema.

TABLE VII

INCIDENCE OF POST-PLASTER OEDEMA AFTER ANKLE FRACTURES

| Type of Fracture | Incidence % |
|---|---|
| Lateral malleolus only (closed reduction only) | 22 |
| Medial malleolus only: | |
| Closed reduction | 14 |
| Open reduction | 40 |
| Lateral and posterior malleoli (closed reduction only) | 15 |
| Lateral and medial malleoli: | |
| Closed reduction | 24 |
| Open reduction | 43 |
| Trimalleolar fractures: | |
| Closed reduction | 35 |
| Open reduction | 90 |

Similar methods were used in the prevention and management of post-plaster oedema following ankle fractures as for oedema following fractures of the shaft described previously (Nichols and Parish, 1959). The routine use of an elastic bandage was again associated with a shorter disability time and a decreased incidence of oedema.

TABLE VIII

EFFECT OF POST-PLASTER OEDEMA ON TOTAL DISABILITY TIME

| | Total Disability Time in Weeks | |
|---|---|---|
| | Without P.P.O. | With P.P.O. |
| Closed reduction (all cases) | 12 | 15 |
| Open reduction (all cases) | 18 | 25 |

The average total disability time of all cases treated as a routine with elastic webbing bandages was 17 weeks, whereas the total disability time for all other cases was 19 weeks.

## ANKLE MOBILIZATION

The average range of ankle movement on removal of plaster was 3 degrees of dorsiflexion and 32 degrees of plantar flexion (the normal range varies from 4 to 25 degrees of dorsiflexion and from 45 to 70 degrees of plantar flexion).

The length of time the ankle was in plaster had no significant effect except in the relatively few cases with the more severe injuries, in which union was delayed more than 12 weeks. Patients with intertubercular fractures of the fibula regained movements much more rapidly than those with any other type

of fracture. There was little difference in the rate of ankle mobilization between bimalleolar and trimalleolar fractures. Five degrees of dorsiflexion, the range required for a limp-free walk, was regained by all patients before discharge, 90% regaining this range by the fourth week of mobilization. Only a few patients failed to regain 45 degrees of plantar flexion (to 135 degrees, the lower range of normal), and 90% achieved this range by the sixth post-plaster week.

Of the whole series, 80% were recorded as having full ankle movements on discharge.

It is interesting to record that on removal of the plaster the range of pronation was frequently greater than that of supination after both diaphysial and ankle fractures, but the difference was much larger in the latter group.

## Recovery of Function

In both diaphysial and malleolar fractures of the tibia and fibula the recovery of function has been assessed by recording (1) the patient's ability to stand on the toes of the injured leg, at first with and later without support; (2) his ability to walk without a limp; and (3) his ability to run.

TABLE IX

Functional Recovery after Ankle Fractures
(Average Time in Weeks after Removal of Plaster)

| | Able to Stand on Toes | Able to Walk Without Limp | Able to Run With Minimal Limp |
|---|---|---|---|
| All malleolar fractures treated at M.R.U. in plaster .. .. .. .. .. | 5 | 6 | 6 |
| All malleolar fractures transferred to M.R.U. immediately after removal of plaster .. .. .. .. .. | 6 | 6 | 6 |
| All malleolar fractures transferred to M.R.U. more than 2 weeks after removal of plaster .. .. .. | 11 | 10 | 12 |

With shaft fractures we found that only patients treated in plaster at a rehabilitation centre for more than one month attained a normal walk *before* they could run with even steps. The remainder could run quite well before they were able to walk without a limp. We concluded this difference was due to the fact that the first group had received supervision in walking correctly in plaster. In 50 patients with malleolar fractures (Parish, 1957) full-time rehabilitation in plaster had no statistically significant effect on recovery of function, but delay

in instituting full-time rehabilitation after removal of the plaster considerably retarded the patient's progress. (See Table IX.)

Recovery rates varied little with the different types of fractures. Bimalleolar and trimalleolar fractures reached each stage approximately one week after unimalleolar fractures. Epiphysial displacement fractures reached each stage approximately two weeks earlier than unimalleolar fractures.

## Complications of Malleolar Fractures

The incidence of soft-tissue complications of 97 diaphysial and 61 malleolar fractures (Parish, 1957) was as follows:

| Complication | Diaphysial Fractures (%) | Malleolar Fractures (%) |
|---|---|---|
| Pes valgus .. .. .. .. | 17 | 25 |
| Tendon lesions .. .. .. | 12 | 1 |
| Metatarsalgia .. .. .. | 11 | 10 |
| Ankle effusion .. .. .. | 8 | 4 |

Pes valgus, metatarsalgia, and ankle effusion were, in the main, transient episodes lasting only a few weeks, but indicate a potential factor in delaying recovery, especially if neglected.

The two main sources of difficulty in rehabilitation of malleolar fractures were: (1) severe disruption of the joint caused by severe trauma (these injuries were rarely isolated); and (2) delayed union or non-union of the medial malleolus and delayed union following supratubercular fracture of the fibula. The following case history illustrates this latter point.

## CASE HISTORY

An officer aged 24 had a ski-ing accident in which he sustained a fracture of the medial malleolus. An attempt was made to reduce the fracture, but eight days after the accident open reduction was carried out. The medial malleolus was found to be rotated. It was reduced and sutured into position. The patient remained in plaster for eight weeks. On removal of the plaster he rapidly regained almost full ankle movements, but he was unable to walk or run because of persistent pain over the fracture site. A radiograph showed incomplete union. Hydrocortisone and local anaesthetic injection relieved symptoms temporarily. It was four months before he was able to walk without a limp, and the subsidence of symptoms and recovery of function coincided with the slow union of the fracture.

He still had some symptoms on discharge six months after the injury.

## DISCUSSION

We have been able to show that the treatment at rehabilitation centres of patients with ankle fractures is particularly valuable during the early post-plaster phase. The main advantage in having these patients at the centres in plaster is that they are available for treatment during this phase. Since weight-bearing through a below-knee plaster starts early in most cases the need for walking training is less important than with long leg plasters, and rehabilitation in plaster does not increase the rate of recovery of walking as with shaft fractures. The principal complications of ankle fractures, which benefit by intensive treatment during the early post-plaster phase, are: (1) oedema; (2) calf-muscle weakness; and (3) localized ankle pain.

Post-plaster oedema was particularly liable to complicate open reduction, especially in bimalleolar and trimalleolar fractures. Although the oedema could be prevented or rapidly controlled by the application of a firm elastic bandage in the early stages, the delayed arrival of the patient with oedema some weeks after removal of the plaster makes it more difficult to ensure dispersion. The incidence of oedema with ankle fractures was greater than that following shaft fractures, but the association of patchy decalcification in radiographs of the tarsus with persistent oedema was not observed. This suggests that different processes were involved in the production of oedema in the two groups. We have suggested previously (Nichols and Parish, 1959) that there might be a connexion between osteoporosis, oedema, and vascular damage with ischaemia, based on the findings of Ellis (1958) regarding the soft-tissue complications of shaft fractures. If this is so, then our present survey suggests that the association applies only to shaft fractures. In ankle fractures dispersion of oedema may be related more directly to the efficiency of the calf-muscle pump.

The development of calf-muscle power has been assessed by graded tests of the ability of patients to stand on the toes, to walk, and to run. A detailed analysis of this process (Parish, 1957) showed that those patients arriving for rehabilitation within the first fortnight after removal of the plaster were able to catch up with the patients treated in plaster in the performance of these tests by about the sixth post-plaster week. However, patients arriving for treatment in later weeks did not show this tendency to catch up with the others.

Calf-muscle power and co-ordination may be severely inhibited by pain in the region of the ankle. Similar retardation of recovery has also been observed with supratubercular fractures of the fibula, when union has been slow. Magnusson (1944, 1945), in a survey of 412 malleolar fractures examined approximately five years after the initial injury, drew attention to the frequency of ununited fractures of the anterior tubercle of the tibia in those fractures in

which osteoarthritis subsequently developed. Several patients with these radiological changes still had persistent swelling and tenderness over the anterior inferior tibio-fibular ligament some years after injury. Using special radiological views, Magnusson found lesions of the anterior tibial tubercle in 65% of malleolar fractures produced by lateral rotation or abduction of the talus, and even following fractures by adduction if gross displacement of the medial malleolus had occurred. This lesion may be of some importance in delaying the recovery of patients with ankle fractures, particularly if they have been inadequately immobilized. Magnusson criticized the short period of immobilization employed in his series of ankle fractures, and recommended longer periods in plaster for the various fracture groups which were very similar to the mean periods recorded in our own series. On the other hand, we have occasionally observed patients with gross displacement and obvious instability of the talus or with non-union of the medial malleolus who have recovered quite rapidly without much discomfort in the ankle.

Good muscle control reduces the effect of residual instability of the ankle, and this can be attained most rapidly by early rehabilitation. There is still a need for further studies of the persistently painful ankle as well as of the best methods of developing calf-muscle power.

## SUMMARY

The results of the rehabilitation of 191 patients with malleolar fractures of the tibia and fibula have been analysed.

The value of transfer of patients to rehabilitation centres for treatment in plaster appears to lie mainly in having patients available for treatment in the immediate post-plaster phase.

Patients arriving at the rehabilitation centre later than the second post-plaster week required considerably longer periods of treatment than the remainder. This difference appeared to be due partly to delay in dispersion of oedema and partly to delay in development of calf-muscle function.

The development of oedema was not associated with osteoporosis seen on the radiographs taken at the time of removal of plaster as had been observed following shaft fractures.

Organized exercises in plaster did not result in quicker return of ability to walk, to "spring", or to run when the plaster was removed.

The main sources of difficulty in rehabilitation of malleolar fractures were: (1) severe disruption of the ankle-joint; (2) pain due to delayed union or non-union of the medial malleolus or delayed union of supratubercular fractures of the fibula.

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GUY'S HOSPITAL MEDICAL SCHOOL

DIPLOMA IN PHYSICAL MEDICINE—PART I

THE next course for this Diploma will commence on Tuesday, January 5, 1960. Full particulars from: Physics Department, Guy's Hospital Medical School, London, S.E.1.

# CENTENARY OF THE DEVONSHIRE ROYAL HOSPITAL, BUXTON

To mark the centenary of the Devonshire Royal Hospital, Buxton, a joint meeting of the Heberden Society and the British Association of Physical Medicine was held at Buxton on July 25 and 26, 1959. It was also attended by members of the Canadian Rheumatism Association, the Canadian Association of Physical Medicine, the Nederlandse Vereniging voor Rheumatologen, and the Manchester Regional Orthopaedic Association.

During the morning of Saturday, July 25, papers were read by members of the Heberden Society and their guests. In the afternoon, papers were read by members of the British Association of Physical Medicine and their guests. On Sunday, July 26, visits were arranged to the Devonshire Royal Hospital, the University Department of Rheumatology and the Empire Rheumatism Council Field Unit at Manchester. A cocktail party and dinner were held at the Palace Hotel, Buxton, on Saturday evening, at which Dr. H. A. Burt, President of the British Association of Physical Medicine, proposed the toast of the Devonshire Royal Hospital. This was replied to by Professor J. H. Kellgren, President of the Heberden Society. Short abstracts of papers presented at the meeting are given below.

## PAPERS BY MEMBERS OF THE HEBERDEN SOCIETY AND THEIR GUESTS

Dr. N. CARDOE: "*Controlled Trial into the Use of G27 202 in Rheumatoid Arthritis.*"

Dr. Cardoe discussed the results of a controlled double-blind trial of a metabolite of phenylbutazone ("butazolidin")—G27 202—when this drug was given for six weeks to a group of 30 patients with rheumatoid arthritis. Patients taking G27 202 had less need of analgesics, a better grip, and less morning stiffness than patients taking the control tablets. No significant side-effects were noted during this short trial of G27 202.

Dr. R. K. W. KUIPERS: "*Adrenal Steroids in Combination with Pyrazolones in the Treatment of Rheumatoid Arthritis, Juvenile Rheumatoid Arthritis, and Ankylosing Spondylitis.*"

Dr. Kuipers described the use of a combination of prednisone and phenylbutazone given in one tablet in the treatment of rheumatoid arthritis, Still's disease, and ankylosing spondylitis. Each tablet contained 1·25 mg. prednisone and 50 mg. phenylbutazone, and the maintenance dose was three or four tablets a day. He claimed that the combination had several advantages over the two drugs given separately, there being fewer side-effects and patients required a lower maintenance dose.

Mr. J. CHARNLEY: "*Experimental Observations on the Lubrication of Joints.*"

Mr. Charnley noted that it was commonly accepted that joint lubrication was hydrodynamic, depending primarily on the presence of a fluid lubricant, synovial fluid, which formed a film between the articular surfaces. Yet no form of hydrodynamic lubrication would account for the low coefficient of friction actually present

in joints when starting motion from rest. Moreover, synovial fluid under experimental conditions was not a good lubricant in an artificial joint. His experiments showed that joint lubrication was not dependent on the presence of synovial fluid in the joint cavity, but on the intrinsic slipperiness of the articular cartilage, and was an example of boundary lubrication. This might account for poor results following arthroplasty where metal replaced articular cartilage. He was investigating the use of an inert plastic, fluon, which had a low coefficient of friction. During the last two years he had used fluon prostheses when performing arthroplasties on rheumatoid patients with good results, and with less new bone formation than was often seen following the use of metal prostheses.

Dr. J. J. DE BLÉCOURT: "*Mobile Physiotherapy in the Netherlands.*"

Dr. J. J. de Blécourt described the formation of a mobile physiotherapy service in Holland intended to treat patients in outlying districts.

During the discussion which followed this paper, several British speakers mentioned their own experience of mobile physiotherapy units. It was generally agreed that they were expensive to run and that in Britain it was better to bring the patient to the hospital than to take physiotherapy to the patient.

Dr. J. N. SWANSON: "*New Techniques of Splint-making—the Prevention and Correction of Deformity in Arthritis using Durafoam Plastic.*"

Dr. J. N. Swanson described the use of a new plastic, Durafoam, which could be moulded directly to the body, as the warmth of the chemical reaction did not exceed that of an ordinary wax bath. It was simple to apply, exceedingly light yet very strong. It was transparent to X rays, could be supplied in attractive colours, which helped to heighten the patient's morale, and could be remoulded by gentle heating to correct deformities.

[Later in the day Dr. Swanson gave an excellent demonstration of the use of Durafoam in making splints. Unfortunately this plastic is not yet available in Great Britain.]

Dr. W. R. M. ALEXANDER and Dr. J. J. R. DUTHIE: "*Studies of the Anti-nuclear Factor in Disseminated Lupus Erythematosus.*"

Dr. Alexander noted that an anti-nuclear factor (A.N.F.) had been demonstrated in the serum of patients with disseminated lupus erythematosus (D.L.E.) by a number of workers, using anti-human-globulin serum conjugated with fluorescein. He described experiments in which sera shown by the above method to contain A.N.F. were conjugated directly with fluorescein without loss of activity. These conjugates were taken up by leucocytes on a dried unfixed blood film, with resulting nuclear fluorescence, but not by leucocytes in suspension. This suggested that undamaged leucocytes did not take up A.N.F. However, A.N.F. was taken up by leucocytes in suspension when exposed to ultra-violet light.

Professor J. H. KELLGREN: "*Report of Medical Research Council and Nuffield Foundation Joint Committee Trial of Prednisolone in Rheumatoid Arthritis.*"

Professor Kellgren reported on a multi-centre controlled trial of prednisolone compared with aspirin or other analgesics in the treatment of rheumatoid arthritis.

The patients treated with prednisolone showed an early significant improvement in both clinical and laboratory indices of inflammatory polyarthritis, and this improvement, though not so marked, was still present to a significant degree at the end of two years. Radiological signs of erosive joint disease in hands and feet progressed significantly in the patients treated with analgesics, but no such progression was observed in the joints of patients treated with prednisolone. In many patients treated with prednisolone the agglutinating titre in the sheep-cell test rose during the two years of treatment, whereas such a rise occurred in only a few patients treated with analgesics. Professor Kellgren noted, but could not explain, this phenomenon, which seemed contrary to the clinical results. Two patients treated with analgesics died of heart failure. Five patients treated with prednisolone developed major complications when taking more than 20 mg. daily; two developed psychoses and three peptic ulceration. Professor Kellgren emphasized, in the discussion which followed this paper, that each case of rheumatoid arthritis must be assessed individually; the results of a two-year trial cannot be applied indiscriminately, in view of the long-term complications of steroid therapy.

Dr. H. DUNCAN and Dr. A. S. DIXON: "*Familial Hyperuricaemia Nephropathy.*"

A builder's labourer aged 19 who came to hospital was found to have mild gout and severe hypertensive renal disease. The question arose whether the gout had caused the renal disease, or the latter, by causing hyperuricaemia, had resulted in secondary gout. A study of the patient's parents and five surviving siblings disclosed that they all had hyperuricaemia; only one brother had gout, but all except two members of the family had renal disease. It was suggested that hyperuricaemia itself might be damaging to the kidneys and that familial hyperuricaemia might be a cause of hypertensive renal disease. It was important to recognize such patients before irreversible renal damage occurred, now that effective uricosuric agents were available.

## PAPERS BY MEMBERS OF THE BRITISH ASSOCIATION OF PHYSICAL MEDICINE AND THEIR GUESTS

Dr. P. HUME KENDALL and Dr. M. E. FEARNLEY: "*Punch Biopsy of the Vertebral Bodies.*"

Dr. Hume Kendall described a technique of aspiration biopsy of vertebral bodies using a specially designed biopsy needle and guide. Twenty successful biopsies were performed under local anaesthesia, patients being suitably premedicated. In twelve patients vertebral biopsy confirmed or altered a clinical diagnosis. In eight patients normal bone was obtained. Dr. Hume Kendall discussed the indications for this procedure in the diagnosis of localized vertebral disease, and emphasized the need for a good knowledge of the anatomy of the spine and a careful technique under radiographic control. In theory, the procedure might be complicated by damage to the spinal cord or large blood-vessels, and aseptic necrosis of the vertebra or seeding of tumours along the needle track might occur. No such complications had yet been reported, and none had occurred in the present series. He concluded that needle biopsy of vertebral bodies might be a valuable diagnostic procedure in a small and selected group of patients.

[It is hoped to publish this paper in full in a later number of the *Annals*.—EDITOR.]

Dr. R. GREENWOOD: "*Circulating Antibody Production in Rheumatoid Arthritis.*"

Dr. Greenwood described the results obtained by immunizing 22 patients with tetanus toxoid and comparing the antitoxin titres with those of similarly immunized control patients. The antitoxin response of the group of patients with rheumatoid arthritis was significantly higher than that of the controls and, though it bore no relationship to the differential agglutination titre, was generally greater in those with active disease. Dr. Greenwood suggested that these results indicated that rheumatoid arthritis was associated with a generally increased activity of the antibody-producing mechanism—a state which would account for the presence of other serological abnormalities, such as increased streptococcal agglutinins, without their being of specific aetiological significance.

Dr. HARRIS: "*Rehabilitation and Resettlement in Rheumatoid Arthritis.*"

Dr. Harris discussed the results of treatment of 988 patients with rheumatoid arthritis who were admitted to the Rehabilitation Unit of the Devonshire Royal Hospital, Buxton, between 1953 and 1958. The majority had suffered from arthritis for several years, but were only recently severely disabled. On admission only 14% were fit for work, whereas 51% were fit for some work on discharge. Follow-up two to three years later showed that over half these patients were resettled satisfactorily. However, Dr. Harris emphasized the difficulty in obtaining work for some of the male patients in an industrial area, as none could be placed in heavy manual work and many could only be resettled in less skilled employment.

Dr. P. BAUWENS: "*Electrodiagnostic Definition of Site and Nature of Peripheral Nerve Lesions.*"

Dr. Bauwens referred to the three conditions generally thought to result from peripheral nerve injury—neuropraxia, axonotmesis, and neurotmesis. Studies of nerve-compression syndromes, however, suggested that two further conditions might occur, both resulting from a progressive obliterating process involving the nerve with a gradual reduction of the cross-section of the axoplasm; local reduction in calibre at the site of the compression might be called "axonostenosis", and if there was, as seemed likely, some reduction in calibre of the entire fibre distal to the compression this might be termed "axonocachexia". A reduction in nerve calibre would result in a rise in the threshold of excitability and a decrease in the velocity of conduction, and this would be detected by electromyography if the affected nerve were stimulated above, and if possible below, the lesion. The site as well as the nature of a peripheral nerve lesion might be determined by examining the myogram.

Dr. Bauwens showed a film illustrating the effect of the various lesions he had described on nerve conduction.

Dr. E. N. COOMES: "*A Correlated Study of Intensity–Duration Curves and Terminal Neuronal Innervation of Muscle.*"

Dr. Coomes discussed the results obtained from studying five cases of chronic lower motor neurone degeneration by correlated muscle biopsy and electrical reactions in an attempt to explain the paradoxical finding of normal electrical reactions in weak and wasted muscles. He concluded that this was due to sprouting of unaffected ultra-terminal axons, which branched to supply denervated muscle fibres

lying in close proximity. Although this sprouting was seen in all lower motor neurone lesions, it was only in slowly progressive cases that this "mopping-up operation" masked the signs of denervation.

[It is hoped to publish this paper in full in a later number of the *Annals*.—EDITOR.]

Dr. C. M. GODFREY: "*The Immobilizing Efficiency of Cervical Braces.*"

Dr. Godfrey discussed the efficiency of different cervical braces and collars in immobilizing the cervical spine by preventing flexion and extension. Radiographs were taken in flexion and extension before and after the patient put on the brace, and these radiographs were superimposed and measurements made from them. Dr. Godfrey concluded that a felt collar was effective only if it was high at the back, and even then it was less effective than a plastic or metal support. A cervical ruff made from Middlesex bandage was more effective than the standard felt or plastic collar.

Mr. J. C. F. CREGAN: "*Simple Correction of Equinus Deformity in Still's Disease by Open Tarsal Crushing.*"

Mr. Cregan described a simple method of correcting an equinus deformity of the foot in patients with the ankylosing form of Still's disease. The tarsal bones were crushed through a dorsal incision and the foot was manipulated into a correct position. These patients formed new bone readily and recovered rapidly from the operation.

S. MATTINGLY

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## ROYAL SOCIETY OF MEDICINE: SECTION OF PHYSICAL MEDICINE

### RICHARD KOVACS PRIZE

THE Council of the Royal Society of Medicine has recently accepted from Mrs. Ina Kovacs, of New York, a sum of money which will make it possible for a Richard Kovacs prize to be awarded triennially in memory of her husband. The prize will be awarded first in 1961, and it will be to the value of £50. It will be awarded by the Council of the Society, on the recommendation of the Council of the Section of Physical Medicine, for distinguished work in physical medicine during the previous three years. The award of the prize may, at the discretion of the Council of the Section, provide an occasion for the reading of a paper by the recipient at a meeting of the Section.

Details of the form which applications for the prize should take will be notified in the medical press later.

# REVIEWS OF BOOKS

POSTURAL DRAINAGE AND RESPIRATORY CONTROL. By E. Winifred Thacker. *Second edition. Pp. 62. 10s. 6d. London: Lloyd-Luke. 1959.*

In the second edition of this small monograph special consideration is given to the principles underlying postural drainage. In the first chapter the anatomy and physiology of the thoracic cage and lungs are dealt with briefly but adequately in simple terms, and the text is amply illustrated by good line diagrams. The technique of postural drainage is described as a logical sequence to the anatomy of the bronchial tree. The procedure for the drainage of each pulmonary segment is dealt with in turn, with accompanying diagrams and photographs. The special problems of postural drainage in the young and in the elderly and emphysematous patient are discussed, but the recommendation that $CO_2$ inhalations may be used to stimulate respiration in the latter group is often untrue and might be dangerous in unskilled hands. Further chapters deal with pre- and post-operative measures in thoracic cases.

This book can be fully recommended to all those who perform or prescribe postural drainage. It contains a wealth of information, and the illustrations are of high quality. D. A. H. YATES

A SYSTEM OF ORTHOPAEDICS AND FRACTURES. By A. Graham Apley. *Pp. 357. 47s. 6d. London: Butterworth. 1959.*

This book is based on a course in orthopaedics and fractures held at Pyrford for many years and designed primarily for F.R.C.S. candidates. Mr. Apley must be an excellent teacher, and the book was undoubtedly written because of the popularity of his lectures. By using note form and short, clear sentences an amazing quantity of material has been compressed into comparatively few pages. The general standard is excellent, giving a well-balanced account of current orthopaedic views. In some sections the material is a summary of a recent outstanding article or monograph; and each chapter is followed by well-selected suggestions for further reading.

There are a few statements in the book with which one could disagree; but the only serious criticism is of chapters, such as those on rheumatoid arthritis and cerebral palsy, in which the subject-matter is so complicated that it cannot be condensed satisfactorily into a few pages. This is one of the penalties of adopting a system. However, the general standard is so good that such difficulties will be readily accepted; and the book can be strongly recommended to medical students, postgraduates studying general surgery or physical medicine, physiotherapists and anyone who has to teach this subject. D. A. BREWERTON

THE CHILD WITH A HANDICAP. By Edgar E. Martmer. *Pp. 397. 82s. 6d. Oxford: Blackwell. 1959.*

Prevention of crippling is axiomatic to the truth that "the cripple is made and not born". The personal observations of no fewer than 27 authoritative contributors have been collated under the editorship of Edgar E. Martmer in this very comprehensive book on the handicapped child. Physical, mental, and emotional problems are equally represented, and it is a welcome sign that child psychiatry has a prominent place in the text. The aim is to get the child vocationally self-reliant, and he and his family optimistic in outlook. Establishing rapport with the parents to enable them to

unburden their problems is stressed as an integral part of the whole subject. The team involved must range from the geneticist and physician to the school-teacher and social worker.

A well-illustrated section on ingenious prostheses for the amputee is described with clarity, and briefly touches on the possibilities with cineplasty. The chapter on poliomyelitis is well written and includes often forgotten possibilities with "frog breathing" and hydrotherapy. Rheumatic fever is dealt with in a way that leaves one with the impression of the author's vast personal experience and concludes with a concise summary. Prophylaxis for life of those who have had rheumatic fever appears to be "sold" in the U.S.A. Much of the philosophizing of the early sections could have been condensed, and it is a loss that the handicaps confronting the asthmatic child are omitted. This could have replaced the chapter devoted to mucoviscidosis, a very small numerical problem compared with asthma.

This book, not primarily a medical textbook, has achieved its object of computing the many facets involved in caring for the child with a handicap.

LESLIE G. ANDREWS

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## THIRD INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE

THE Third International Congress of Physical Medicine, under the Presidency of DR. Frank H. Krusen, will take place in Washington, D.C., from August 21 to 26, 1960. The Hon. Richard M. Nixon, Vice-President of the United States, is patron of the Congress. A preliminary outline of the scientific programme is as follows:

*Monday, August 22.*

2 p.m. Diagnosis, Evaluation, and Treatment of Diseases of Skeletal Muscle.

*Tuesday, August 23.*

9 a.m. Arthritis and Collagen Diseases.

2 p.m. Neuromuscular Diseases.

*Wednesday, August 24.*

9 a.m. Physiatric Care following Trauma to the Neuromuscular and Musculoskeletal System.

Noon Open for tours in Washington and surrounding areas.

*Thursday, August 25.*

9 a.m. Evaluation, Prevention, and Treatment of Scoliosis.
Congenital Defects causing Physical Disability.

2 p.m. Rehabilitation following Amputation.

*Friday, August 26.*

9 a.m. Geriatric Care.
Closing ceremony.

2 p.m. Final business meeting of International Federation.

In addition, there will be a social programme and a post-Congress tour to Williamsburg, Richmond, Philadelphia, and New York.

Members of the British Association of Physical Medicine who have not yet obtained a preliminary programme should apply to the Secretary, Third International Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois, U.S.A.

# ABSTRACTS OF THE LITERATURE

**Antibody Response in Adolescents and Adults to a Booster Dose of Poliomyelitis Vaccine.** MEDICAL RESEARCH COUNCIL REPORT. *Brit. med. J.*, 1959, **1**, 609.

**Management of Poliomyelitis.** W. RITCHIE RUSSELL. *Brit. med. J.*, 1959, **1**, 613.

**Some Diagnostic Problems surrounding Poliomyelitis.** J. F. GALPINE. *Brit. med. J.*, 1959, **1**, 616.

**Epidemiology of Poliomyelitis.** G. W. A. DICK. *Brit. med. J.*, 1959, **1**, 618.

**Present Situation with Formalin-killed Poliomyelitis Vaccine.** J. KNOWELDEN. *Brit. med. J.*, 1959, **1**, 620.

The first of this group of papers reports work undertaken by the Biological Standards Control Laboratory of the Medical Research Council. The other papers were presented to the Section of Medicine at the annual meeting of the British Medical Association at Birmingham in 1958.

The report from the Medical Research Council suggests that a threefold increase in the amount of Type 1 antigen in poliomyelitis vaccine will be necessary to give satisfactory antibody responses after three doses in all subjects.

Dr. Ritchie Russell discusses the management of respiratory paralysis in poliomyelitis. He describes the indications for intermittent positive-pressure respiration and makes a plea for early assistance of respiration, both in respiratory-muscle and bulbar paralysis, before the patient has become too anoxic or distressed. He advocates two-hourly passive joint movements from an early stage, and encourages voluntary activity within two or three weeks of the acute stage.

Dr. Galpine discusses the diagnosis of the non-paralytic form of the disease, with particular reference to other viruses which may mimic it. He also deals with the problem of polioencephalitis and its clinical recognition.

Dr. Dick discusses the epidemiology of the disease, and points out that there are "hot" families who are good disseminators of the virus and "cold" families who are poor disseminators. He suggests that the siblings of a paralysed child should be quarantined for a week.

Dr. Knowelden draws attention to the lack of knowledge concerning the length of time vaccination will be protective and discusses the number and spacing of inoculations.

[These are all interesting papers and are worth studying, as they represent an up-to-date appreciation of the position by experts in their fields.]

C. B. WYNN PARRY

**Studies on the Mechanism of the Lupus Erythematosus (L.E.) Phenomenon.** A. C. AISENBERG. *J. clin. Invest.*, 1959, **38**, 325.

The studies here reported suggest that a two-stage process is concerned in the formation of L.E. cells. The first stage, specific for patients with lupus erythematosus, involves the reaction of a component of the cell nucleus with the L.E. factor and the morphological alteration of the nucleus associated with this reaction. Isolated nuclei obtained by cell fractionation are used in this experiment. The second stage is the phagocytic step in which the altered nuclear material is phagocytosed by normal white cells to give L.E. cells. This step involves a heat-labile factor present in normal serum, believed to be a phagocytosis-promoting co-factor.

By the use of a quantitative technique it is shown that nuclei will take up more L.E. than normal gamma globulin, and L.E. factor in various patients is not identical. It is conjectured that the varied clinical picture of lupus erythematosus disseminatus is a reflection of the variation in the L.E. factor in different patients. Evidence is produced suggesting that the L.E. factor reacts with the non-histone protein rather than the deoxyribose nucleic acid of the nucleus, which is contrary to the work of other investigators.

MAURICE F. HART

**Congenital Insensitivity to Pain: A Neurologic Syndrome with Bizarre Skeletal Lesions.** F. N. SILVERMAN and J. J. GILDEN. *Radiology*, 1959, **72**, 176.

Cases are reported of three sisters with lesions of the bones which were thought to represent repetitive unrecognized trauma of the bones and the result of congenital insensitivity to pain. The other features of this condition are discussed and the literature reviewed.

G. O. STOREY

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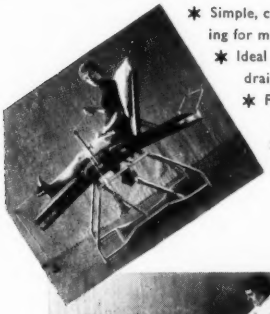

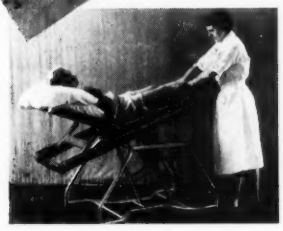

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